Amendments to the Specification:

Applicant respectfully requests that the following paragraphs be replaced in the specification.

Page 5, lines 25 through page 6, line 7:

In a preferred embodiment of the first aspect of the invention, the target cell-specific portion comprises an humanised HMFG-1 monoclonal antibody or an antigen binding fragment thereof. HMFG antibodies are raised against human milk fat globule (HMFG), in a delipidated state (see Taylor-Papadimiriou *et al.*, 1981, *Int. J. Cancer* **28**:17-21 and Gendler *et al.*, 1988, *J. Biol. Chem.* **236**:1282-12823). HMFG-1 monoclonal antibodies bind to a particular component of HMFG, namely polymorphic epithelial mucin (PEM). Binding is thought to involve the amino acid sequence APDTR (SEQ ID NO: 101) within the twenty amino acid tandem repeats of the *muc-1* gene product.

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Page 8, lines 14-16:

Yet more preferably, the target cell-specific portion comprises an amino acid sequence encoded by at last part of one or both of the nucleotide sequences of Figure 3(a) (SEQ ID NO: 7) and (d) (SEQ ID NO: 10).

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Page 8, lines 18-20:

Most preferably, the target cell-specific portion comprises an amino acid sequence encoded by the nucleotide sequence of Figure 3(a) (SEQ ID NO: 7) and

A3

A3 an amino acid sequence (SEQ ID NO: 12) encoded by the nucleotide sequence of Figure 3(d) (SEQ ID NO: 11).

Page 9, lines 3-8:

Preferably, the target cell-specific portion comprises an antigen binding fragment of an humanised HMFG-1 monoclonal antibody, *e.g.* an Fab or $F(ab')_2$ fragment thereof, wherein a hinge region contains a mutation (*i.e.* wherein the hinge is a variant or hybrid of a naturally occurring hinge). More preferably, the variant hinge comprises the amino acid sequence CCVECPPCPAPE (SEQ ID NO: 100).

Page 9, line 27 through page 10, line 2:

More preferably, the endonuclease is a human deoxyribonuclease I. Most preferably, the cytotoxic portion comprises the amino acid sequence shown in Figure 2(a) (SEQ ID NO: 4) or 2(b) (SEQ ID NOS: 6).

Page 11, line 26 through page 12, line 5:

Preferably, the nuclear localization signal (NLS) comprises a nuclear localization signal from the SV40 large T antigen (Kalderon *et al.*, 1984, *Cell* **39**:499-509), and specifically the amino acid sequence PKKKRKV (SEQ ID NO: 96). Inclusion of a nuclear localization signal encourages the compound of the invention to gain access to the chromosomal DNA during the periods of the cell cycle when the nuclear membrane is intact, since the nuclear pores are permeable to large molecules incorporating said nuclear localization signal.

Page 12, line 26:

Most preferably the linker sequence is or comprises GG or GSGG (SEQ ID NO: 97).

Page 13, lines 12-18:

In a preferred embodiment of the first aspect of the invention, the compound comprises all or part of the amino acid sequence as shown in Figure 3(c) (SEQ ID NO: 9) (*i.e.* an HMFG-1 light chain) together with all or part of an amino acid sequence selected from the group consisting of amino acid sequences as shown in Figures 5(d) (SEQ ID NO: 38), 6(d) (SEQ ID NO: 43), 7(b) (SEQ ID NO: 46), 8(b) (SEQ ID NO: 49), 9(b) (SEQ ID NO: 52), 10(b) (SEQ ID NO: 55), 11(b) (SEQ ID NO: 58), 12(b) (SEQ ID NO: 61), 13(d) (SEQ ID NO: 66), 14(d) (SEQ ID NO: 71), 15(d) (SEQ ID NO: 76), 16(c) (SEQ ID NO: 80), 17(d) (SEQ ID NO: 85), 18(d) (SEQ ID NO: 90) and 19(d) (SEQ ID NO: 95) (*i.e.* an HMFG-1 heavy or Fd chain/DNase fusion).

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Page 13, lines 20-24:

Advantageously, the compound is a whole HMFG-1 antibody/human DNase I fusion compound comprising an amino acid sequence as shown in Figure 3(c) (SEQ ID NO: 9) and an amino acid sequence as shown in Figure 7(b) (SEQ ID NO: 46). Preferably, the compound is a tetrameric compound comprising two HMFG-1 light chains and two HMFG-1 heavy chain /DNase I fusions.

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Page 13, lines 26-27:

A10 Conveniently, the compound comprises an amino acid sequence as shown in Figure 3(c) (SEQ ID NO: 9) and an amino acid sequence as shown in Figure 14(d) (SEQ ID NO: 71).

Page 14, lines 20-27:

In a preferred embodiment of the second aspect of the invention, the nucleic acid molecule comprises all or part of the nucleotide sequence as shown in Figure 3(a or b) (SEQ ID NOS: 7 or 8) (*i.e.* encoding an HMFG-1 light chain)

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together with all or part of a nucleotide sequence selected from the group consisting of nucleotide sequences as shown in Figures 5(a, b and c) (SEQ ID NOS: 34, 35, and 36), 6(a, b and c) (SEQ ID NOS: 39, 40, and 41), 7(a) (SEQ ID NO: 44), 8(a) (SEQ ID NO: 47), 9(a) (SEQ ID NO: 50), 10(a) (SEQ ID NO: 53), 11(a) (SEQ ID NO: 56), 12(a) (SEQ ID NO: 59), 13(a, b and c) (SEQ ID NOS: 62, 63, and 64), 14(a, b and c) (SEQ ID NOS: 67, 68, and 69), 15(a, b and c) (SEQ ID NOS: 72,73, and 74), 16(a and b) (SEQ ID NOS: 77 and 78), 17(a, b and c) (SEQ ID NOS: 81, 82, and 83), 18(a, b and c) (SEQ ID NOS: 86, 87, and 88) and 19(a, b and c) (SEQ ID NOS: 91, 92, and 93) (*i.e.* encoding an HMFG-1 heavy or Fd chain/DNase fusion).

Page 15, lines 1-3:

Advantageously, the nucleic acid molecule comprising a nucleotide sequence as shown in Figure 3(b) (SEQ ID NO: 8) and a nucleotide sequence as shown in Figure 7(a) (SEQ ID NO: 44).

Page 15, lines 5-6:

Conveniently, the compound comprises a nucleotide sequence as shown in Figure 3(b) (SEQ ID NO: 8) and a nucleotide sequence as shown in Figure 14(c) (SEQ ID NO: 69).

Page 18, lines 21 through page 19, line 1:

Generally, the nucleic acid is inserted into an expression vector, such as a plasmid, in proper orientation and correct reading frame for expression. If necessary, the nucleic acid may be linked to the appropriate transcriptional and translational regulatory control nucleotide sequences recognised by the desired host, although such controls are generally available in the expression vector. For example, the nucleic acid molecule encoding a compound of the invention may be linked to or comprise a Kozak consensus ribosome binding sequence (such as GCCGCCACC)

A14 (SEQ ID NO: 98) to enhance translation.

Page 28, line 4:

Figure 1 shows the complete coding sequence of human DNAse I (SEQ

A15 ID NOS: 1 and 2).

Page 28, lines 6-9:

DNA A3

Figure 2 shows (A) the mature DNAse peptide I (SEQ ID NO: 4)

A16 sequence used in the exemplary Ab-DNase and Fab-DNase constructs, and (B) a truncated DNAse peptide I sequence (SEQ ID NO: 6) encoded by a nucleotide sequence comprising a Kozak sequence (underlined) .

Page 28, lines 11-16:

Figure 3 shows (A) the nucleotide sequence encoding the humanised HMFG1 light chain including leader peptide (SEQ ID NO: 7), (B) the nucleotide sequence of (A) further comprising a Kozak sequence (underlined) (SEQ ID NO: 8),

A17 (C) the amino acid sequence of the humanised HMFG1 light chain including leader peptide (shaded) (SEQ ID NO: 9) and (D) the nucleotide sequence encoding the humanised HMFG1 heavy chain including leader peptide (SEQ ID NO: 10).

Page 28, lines 18-21:

Figure 4 shows the linker and hinge-linker oligonucleotides used in (A) the whole antibody-DNase (SEQ ID NOS: 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 and 24) (B) the Fd-DNase exemplary constructs (SEQ ID NOS: 25, 26, 27, 28, 29, 30,

A18 31, 32, and 33). Note, in Figure 4(A) a deletion of one or more codons between the HMFG1 hinge and the linker is represented as ΔG.

Page 28, lines 23-28:

~~Figure 5~~ shows nucleotide sequences (A and B) (SEQ ID NOS: 34 and 35) encoding a humanised HMFG-1 Fd/DNase I fusion pAS23 comprising a leader sequence (underlined) and a linker sequence (double-underlined). Figure 5(C) shows the nucleotide sequence of (B) further comprising a Kozak sequence (underlined) (SEQ ID NO: 36). Figure (D) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion (SEQ ID NO: 38).

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Page 29, lines 1-6:

Figure 6 (A), (B) and (C) (SEQ ID NOS: 39, 40, and 41) shows the nucleotide sequences of Figure 5 (A), (B) and (C) (SEQ ID NOS: 34, 35, and 36), respectively, further comprising an SV40 NLS (double underlined) (pAS27). Figure (D) (SEQ ID NO: 43) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion comprising an SV40 NLS (double underlined).

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Page 29, lines 8-11:

Figure 7 shows (A) the nucleotide sequence (SEQ ID NO: 44) and (B) the translated amino acid sequence (SEQ ID NO: 45) of an exemplary HMFG-1 heavy chain/DNase I fusion pAS34 (as used in 'Ab-DNase' in Example 2), comprising a leader sequence (underlined) and a linker sequence (double-underlined).

A21

Page 29, lines 13-17:

Figure 8 shows (A) the nucleotide sequence (SEQ. ID NO. 47) and (B) the translated amino acid sequence of an exemplary HMFG-1 heavy chain/DNase I fusion pAS35 (SEQ. ID NO. 48), comprising a leader sequence (underlined) and a linker sequence (double-underlined). The lower case 'g' represents a silent mutation caused by PCR amplification.

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Page 29, lines 19-23:

A23

Figure 9 shows (A) the nucleotide sequence (SEQ. ID NO. 50) and (B) the translated amino acid sequence (SEQ. ID NO. 52) of an exemplary HMFG-1 heavy chain/DNase I fusion pAS36, comprising a leader sequence (underlined) and a linker sequence (double-underlined). The lower case 'c' represents a silent mutation caused by PCR amplification.

Page 29, lines 25-28:

A24

Figure 10 shows (A) the nucleotide sequence (SEQ. ID NO. 53) and (B) the translated amino acid sequence (SEQ. ID NO. 55) of an exemplary HMFG-1 heavy chain/DNase I fusion pAS37, comprising a leader sequence (underlined), a linker sequence (double-underlined) and an NLS sequence (triple underlined).

Page 30, lines 1-6:

A25

Figure 11 shows (A) the nucleotide sequence (SEQ. ID NO. 56) and (B) the translated amino acid sequence (SEQ. ID NO. 58) of an exemplary HMFG-1 heavy chain/DNase I fusion pAS38, comprising a leader sequence (underlined), a linker sequence (double-underlined) and an NLS sequence (triple underlined). The lower case 'g' represents a silent mutation caused by PCR amplification.

Page 30, lines 8-12:

A26

Figure 12 shows (A) the nucleotide sequence (SEQ. ID NO. 59) and (B) the translated amino acid sequence (SEQ. ID NO. 61) of an exemplary HMFG-1 heavy chain/DNase I fusion pAS39, comprising a leader sequence (underlined), a linker sequence (double-underlined) and an NLS sequence (triple underlined). The lower case 'c' represents a silent mutation caused by PCR amplification.

Page 30, lines 14-19:

Figure 13 shows nucleotide sequences (A and B) (SEQ. ID NOS. 62 and 63) encoding a humanised HMFG-1 Fd/DNase I fusion pAS101 comprising a short leader sequence (underlined) and a linker sequence (double-underlined). Figure 13(C) shows the nucleotide sequence (SEQ. ID NO. 64) of (B) (SEQ. ID NO. 63) further comprising a Kozak sequence (underlined). Figure (D) shows the amino acid sequence (SEQ. ID NO. 76) of a humanised HMFG-1 Fd/DNase I fusion.

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Page 30, lines 21-27:

Figure 14 shows nucleotide sequences (A and B) (SEQ. ID NOS. 67 and 68) encoding a humanised HMFG-1 Fd/DNase I fusion pAS102 comprising a leader sequence (underlined) and a hybrid hinge + linker sequence (double-underlined). Figure 14(C) shows the nucleotide sequence (SEQ. ID NO. 69) of (B) (SEQ. ID NO. 68) further comprising a Kozak sequence (underlined) (construct designated pAS302 in Example 2). Figure (D) shows the amino acid sequence (SEQ. ID NO. 76) of a humanised HMFG-1 Fd/DNase I fusion.

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Page 31, lines 1-6:

Figure 15 shows nucleotide sequences (A and B) (SEQ. ID NOS. 72 and 73) encoding a humanised HMFG-1 Fd/DNase I fusion pAS103 comprising a leader sequence (underlined) and a hybrid hinge + short linker sequence (double-underlined). Figure 15(C) shows the nucleotide sequence (SEQ. ID NO. 74) of (B) (SEQ. ID NO. 73) further comprising a Kozak sequence (underlined). Figure (D) (SEQ. ID NO. 76) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion.

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Page 31, lines 8-13:

Figure 16 shows nucleotide sequences (A and B) (SEQ. ID NOS. 77

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and 78) encoding a humanised HMFG-1 Fd/DNase I fusion pAS104 comprising a leader sequence (underlined) and a hybrid hinge + mutated short linker sequence (double-underlined). Figure (C) (SEQ. ID NO. 80) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion. Mutations (compared to pAS103) at positions 775 and 924 are shaded.

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Page 31, lines 15-21:

Figure 17 shows nucleotide sequences (A and B) (SEQ. ID NOS. 81 and 82) encoding a humanised HMFG-1 Fd/DNase I fusion pAS105 comprising a leader sequence (underlined), a short linker sequence (double-underlined) and an NLS sequence (triple underlined). Figure 17(C) (SEQ. ID NO. 83) shows the nucleotide sequence of (B) (SEQ. ID NO. 82) further comprising a Kozak sequence (underlined). Figure (D) (SEQ. ID NO. 85) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion.

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Page 31, 23 through page 32, line 1:

Figure 18 shows nucleotide sequences (A and B) (SEQ. ID NOS. 86 and 87) encoding a humanised HMFG-1 Fd/DNase I fusion pAS106 comprising a leader sequence (underlined), a hybrid hinge + linker sequence (double-underlined) and an NLS sequence (triple underlined). Figure 18(C) (SEQ. ID NO. 88) shows the nucleotide sequence of (B) (SEQ. ID NO. 87) further comprising a Kozak sequence (underlined). Figure (D) (SEQ. ID NO. 90) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion.

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Page 32, lines 3-9:

Figure 19 shows nucleotide sequences (A and B) (SEQ. ID NOS. 91 and 92) encoding a humanised HMFG-1 Fd/DNase I fusion pAS107 comprising a leader sequence (underlined), a hybrid hinge + short linker sequence (double-

A33

underlined) and an NLS sequence (triple underlined). Figure 19(C) (SEQ. ID NO. 93) shows the nucleotide sequence of (B) (SEQ. ID NO. 92) further comprising a Kozak sequence (underlined). Figure (D) (SEQ. ID NO. 95) shows the amino acid sequence of a humanised HMFG-1 Fd/DNase I fusion.

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Page 37, line 25 - Page 38, line 6:

The concentration of constructs in supernatants from transiently transfected L761H cells was determined in a PDTRP-binding ELISA. To each well of a Maxisorb 96-well ELISA plate (Nunc) was added 100 µl of carbonate buffer containing 100 ng of recombinant GST-$(PDTRP)_7$ fusion protein (SEQ. ID NO. 99) (Gendler *et al.*, 1990, *J. Mol. Biol.* **265**:15286-93). After overnight binding at 4°C, the plate was washed three times in PBS-Tween (*i.e.* PBS containing 0.05% Tween-20). The plate was then blocked with three 3-minute washes of PBS-Tween containing 1% BSA.

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Please replace the Sequence Listing as originally provided with pages numbered 1 –150 submitted herewith.